Pregnancy And Diabetes

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The Populations residing in South Asia are unique in many ways. Of the 142 million children born in the world, 88% are born in the developing world. Only 82% would survive to 1 year in developing countries compared to developed countries wherein nearly all would survive. Only 44% of the children complete the primary education in the developing world, rest would have died from one cause or other.

Coming to South East Asia specifically, 30% of all the world's unimmunised and 40% of world's malnourished children live in the three countries: India, Bangladesh and Pakistan. I am highlighting these facts here, because later in this article implications of malnourishment to diabetes will be brought out.

In Asia, one third of children born have low birth weight. This brings out the extent of the problem of maternal and child health care with relation to maternal malnutrition in these countries.

It is along the Equator that the highest prevalence of diabetes is being reported. In India and Indians abroad, the prevalence is at least 10% according to latest figures as compiled by WHO and IDF. This reflects the magnitude of the problem.

In Caucasian population the prevalence is between 2 and 4%. Diabetes mellitus or Impaired Glucose Tolerance (IGT) are absent or rare in some Melanesian Populations, rural Bantu (Tanzania) and Mapuche Indians (Chile). Mexican American have an incidence of 15-20%; in Pima Indians it is 25-55%. Thus, we are very definitely in a pre-explosive phase of diabetes.

In some developing countries, 15% of births are associated with diabetes-related pregnancy. 20% of the macrosomics are born in this region in hospital settings. Immaturity is close to 10% and, fetal and neonatal death 30%. Though children born of diabetes-related pregnancy look large and big, they are not healthy. Shoulder dystocia at birth and respiratory distress are amongst few pathological states observed in such new borns.

Diabetic pregnant women as well as gestational diabetics may give birth to small babies. Major anomalies like sacral dysgenesis and imperforate anus may be observed in such instances. This occurs at the gestational age of 3 weeks. Cardiac anomalies occur between 5 and 6 weeks and renal anomalies occur between 4 and 5 weeks. Increased D-glucose concentration causes embryogenic dysmorphism in-vitro by generation of free oxygen radicals. In order to prevent these complications, diabetes should be detected and treated before the start of pregnancy.

The second characteristic of the infant of diabetic mother or infant of mother with gestational diabetes is hypertrophy and hyperplasia of islets of Langerhans. A linear relationship between the birth weight and islet cell tissue mass in the pancreas exists.

One of the characteristics of these large for date infants of diabetic mothers is related to the alterations in the fetal pancreas; not only the structure, but also as regards the function of islets. Such beta cells during fetal and neonatal life secrete excess of insulin than required. Japanese investigators have shown that infants with birth weight more than 4 kg have hyperinsulinemia as well as increased IGF_1 levels in their cord blood.

In infants who are small for date, the insulin secretion is very definitely much less than that in the healthy infants. It indicates the sensitivity of the beta cell in its structure and function. The alterations in the maternal metabolism inturn influence the beta cell of the fetus- a special target of the intermediary metabolic changes. The fetus attempts to adapt to the maternal metabolism.

The nutrients, especially glucose and aminoacids can traverse the placenta, thus raising the concentration of these nutrients in the fetus and stimulating fetal insulin secretion. This results in accumulation of fats in large for date babies. When HbA_{1c} is high, in turn 2, 3, DPG is low and thus oxygenation is low, the placenta therefore undergoes compensatory changes and assumes a large size. The blood flow consequently is insufficient and that becomes the reason for associated immaturity.

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Another important issue is the development of antibodies to insulin, Islet cell Antibody (ICA) and insulin antibody (IA) freely cross the placenta in IDDM and GDM. These antibodies usually disappear 9 months after birth in the offspring of diabetic mother. It may be hypothesized that transient antibody positivity of both ICA and IA in offspring of diabetic mothers may protect the fetus from developing IDDM in later life. These antibodies are going to capture the insulin that is being secreted by the fetus and is also going to affect the insulin status of the fetus. The fetus is exposed to higher insulin levels and risk of macrosomia, respiratory distress syndrome, hyperbilirubinemia and hyperglycemia. It is important thus to target the treatment with purified, least antigenic insulin such as human insulin to women especially adolescent girls, as soon as they are diagnosed diabetic.

Infant mortality results in increased high blood sugar of the diabetic mother. Infant mortality rate (IMR) is 60-70% if the woman experiences ketoacidosis during pregnancy. Physicians, obstetricians, and paediatricians have come to realise that the near normal the maternal blood sugar the lesser is the infant mortality. This means that the infant mortality is related to the maternal blood glucose states. The steps to achieve normalisation of blood sugar before and during pregnancy started around 1955 in certain centres. It took 25 years (1980) before all the different specialised centres became convinced of its benefits. In this slowness of action nearly two generations have been lost.

Different specialised centres have evolved characteristic approach in management of diabetes programmes. There should be a close collaboration between the obstetrician, the physician and the perinatologist. Without this collaboration it is a losing game; with it, it is a winning team for the betterment of mother and her infant. These centres employ high technology measurements so we can evaluate the exact growth of the fetus; quantitate the fat around the abdomen of the fetus; and state of its increase over a period of time; so as to judge very precisely whether the treatment given is optimal.

In the developed part of the world pregnancy is allowed to proceed till about 39 to 39. 5 weeks. Monitoring by echotomography, echocardiography and blood glucose value assists to achieve this success.

An abnormal blood glucose value during pregnancy is a remarkable marker for the future development of diabetes in woman. 45% of pregnant women with 2-hour post prandial glucose level between 160-179 mg/dl would develop diabetes in the next 4-8 years period.

Also the blood glucose of the mother is very important determinant of diabetes in offsprings. When mother had no diabetes, the 2 hour post prandial blood glucose of offsprings at age 10-14 years is 97 mg/dl as compared to offsprings of diabetic mothers, whose blood glucose will be 130 at the same age. At the age 15-19 the blood glucose of offsprings of diabetic mother will be in the diabetic range.

The blood glucose of the mother with NIDDM is of major importance for the neonate/infant/offspring as it effects the pancreatic development. Thus we have a major responsibility for both the mother and for the infant. In prevention of diabetes one emphases change of environment, change of diet and change of life style; but the first environment that really matters is the intrauterine environment.

Because malnutrition affects the growth of the fetus we studied pregnant rats and the effect of protein content of diet on the growth of the pups. 9% protein instead of 20% protein was given to these animals. We analysed the effect of this diet on fetal endocrine pancreas. We analysed the islet cell proliferation and multiplication of beta cell culture. We also studied islet size, pancreatic insulin content and islet vascularisation.

We observed that pups of mothers on low protein diet had low islet cell proliferation, islet size was reduced, pancreatic insulin content was very low and islet vascularisation was very much affected. There was 60% reduction in islet vascularisation. In addition we analysed the function of these islets at 70 days of life. Insulin levels in such rats was lower. In addition the density of endocrine tissue in pancreas at 70 days of age was only 60% in offsprings of mothers getting low protein diet compared to the offsprings of mothers getting normal protein diet. The effect on the beta cells is also evidenced by low insulin levels and impaired OGTT upto 70 days.

In developing countries infectious diseases play a very important role. The vaccination against the infectious disease is not universal. Thus pregnancy may be affected by congenitial rubella and other viral diseases. This and congenital CMV infection can cause diabetes by affecting the pancreas.

Thus prevention of diabetes should start at the level of intrauterine environment. This includes the maintanence of metabolic milieu and the immunisation against the infectious diseases during pregnancy. Breast feeding seems to be as well important as the incidence of diabetes in the breast fed infants is being reported to be lower than those fed on cow's or formula milk.

I would end by stating that pregnancy and gestational diabetes in developing countries accounts for a major share of world's load of the diabetes issue and explosion. Hence, an awareness of diabetes should be created at the primary health care centres in the developing world. Knowledge that infectious diseases may have a role in causing diabetes has to be recognised and pregnant woman protected by appropriate vaccinations. Screening for diabetes before and during pregnancy would certainly initiate early steps in management. Team-care has reduced maternal and perinatal mortality and complications in diabetic mothers and the new born considerably.

REFFERENCES

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